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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,739	11/18/2003	Murugan R. Pandian	A-1789div	6774

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EXAMINER	
COUNTS, GARY W	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 03/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/716,739	PANDIAN ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-25 and 42-50* is/are pending in the application.

4a) Of the above claim(s) *45-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-25 and 42-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The response to the Election/Restriction filed 01/10/05 and the amendment filed 09/30/04 is acknowledged and has been entered.

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 23-25 and 42-44 in the reply filed on 01/10/05 is acknowledged. The traversal is on the ground(s) that there would be no burden on the Examiner to search or examine the claims of Groups I and II if they were grouped together. Applicant argues that both groups are drawn to methods for detecting a trophoblastic disease in a subject and that both groups of claims contain the steps of (i) contacting a biological sample obtained from subject with antibodies that bind hyperglycosylated human chorionic gonadotropi; (ii) confirming the subject is not pregnant; and (iii) determining an amount of hyperglycosylated human chorionic gonadotropin present in the sample. This in not found persuasive because as stated in the previous office action Invention I involves antibodies for human chorionic gonadotropin and determining an amount of human chorionic gonadotripin and also involves comparing the determined amount of human chorionic gonadotropin present in the sample to a 50^{th} percentile of amounts of human chorionic gonadotropin present in samples obtained from subjects who do not have a trophoblastic disease and Invention II does not require these limitations. Also, Invention II requires that an amount of hyperglycoslyated human chorionic gonadotropin greater than about 400,000 ng/ml indicate the presence of a trophoblastic disease and Invention I does not require this

limitation. Therefore, the inventions are independent and distinct and while the searches may be expected to overlap, there is no reason to expect the searches to be coextensive.

The requirement is still deemed proper and is therefore made FINAL.

Rejections withdrawn

The 112 first rejection of claims 23-25 as failing to comply with the written description requirement is withdrawn in view of the amendments to the claims and applicant's statement that "the antibodies bind to hyperglycosylated human chorionic gonadotropin (hyperglycosylated hCG) or human chorionic gonadotropin. The hyperglycosylated hCG recognized by the antibodies in the claims is a glycoprotein hormone secreted by trophoblast cells" the hyperglycosylated hCG recognized by the antibodies in the claims.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 23-25 and 42-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23, lines 3-5 is vague and indefinite because it is unclear if the antibodies bind to both hyperglycosylated human chorionic gonadotropin and human chorionic gonadotropin or if there are two different antibodies, one specific for hyperglycosylated

human chorionic gonadotropin and one specific for human chorionic gonadotropin. Please clarify.

Claim 23, line 21 "the standards" there is insufficient antecedent basis for this limitation. It is unclear if Applicant is referring to the subjects who do not have a trophoblastic disease or if Applicant is referring to something else. Please clarify.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 23-25, 42 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'connor et al (US 6,500,627) in light of Birken et al (Immunochemical measurement of Early Pregnancy Isofoms of hCG: Potential Applications to Fertility Research, Prenatal Diagnosis, and Cancer, 32 (2001) 635-643) in view of Hochstrasser et al (US 2003/0157580) and Birken et al (US 6,521,416).

O'Connor et al (US 6,500,627) disclose methods of detecting trophoblastic disease. O'Connor et al disclose that the trophoblastic disease can include choriocarcinoma or hydatidiform mole. O'Connor et al disclose contacting a sample from a subject with an antibody which specifically binds to a molecular isoform of hCG. O'Connor et al disclose contacting the sample with a second antibody which specifically binds to intact non-nicked hCG (hCG) (col 4 and col 25-26). O'Connor et al disclose B152 antibodies specific for the isoform of hCG (col 10, lines 40-44). Birken et al (Archives of Medical Research, 2001, 635-643) disclose that B152 is hyperglycosylated form (abstract). Therefore, O'Connor et al teaches detecting hyperglycosylated hCG. O'Connor et al disclose that the amount of B152 isoform (hyperglycosylated hCG) and hCG are increased in trophoblast disease (col 25-26). O'Connor et al also disclose that hCG is elevated in pregnancy. O'Connor et al discloses that the sample can be a blood or urine sample. O'Connor et al disclose that detection can be performed by using an labeled antibody. O'Connor et al disclose that the label can be a radioactive isotope such as I^{125}.

O'Connor et al differ from the instant invention in failing to teach confirming the subject is not pregnant. O'Connor et al also differs from the instant invention in failing to teach comparing the determined amount of hyperglycosylated human chorionic gonadotropin present in the sample to sample obtained from subjects who do not have a trophoblastic disease and comparing the determined amount of human chorionic gonadotropin present in the sample to amounts obtained from subjects who do not have a trophoblastic disease.

Since O'Connor et al discloses that hyperglycosylated hCG and hCG are elevated in both trophoblastic disease and pregnancy one of ordinary skill in the art would consider that pregnancy would have to be excluded before determining trophoblastic disease and thus would confirm that the patient was not pregnant before determining trophoblastic disease. Further, Hochstrasser et al (abstract & page 1, paragraph 0012) teaches that in order to perform diagnostic assays on markers which are known to be involved in more than one condition, one must be able to distinguish between the two and thus perform an assay to exclude one of the conditions. Therefore, it would have been obvious to one of ordinary skill in the art to confirm that the subject is not pregnant before detecting a trophoblastic disease.

Birken et al (US 6,521,416) discloses that analysis of the metabolites of gonadotropins in a sample can help to distinguish between healthy and abnormal physiological states. Birken et al (US 6,521,416) discloses thresholds to determine abnormal states (col 2, line 54 – col 3 , line 14). Birken et al disclose comparing the sample to normal subjects to determine the abnormal state.

It would have been obvious to one of ordinary skill in the art to incorporate thresholds and samples from normal subjects as taught by Birken et al (US 6,521,416) into the method of O'Connor et al because Birken et al shows that this provides for the analysis of the metabolites of gonadotropins in a sample to distinguish between healthy and abnormal physiological states.

With respect to the a 50th percentile as recited in the instant claims, the optimum threshold in this case 50th percentile can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Also, one of ordinary skill in the art would optimize the assay to minimize the false positive and false negative results.

8. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over O'connor et al (US 6,500,627) in light of Birken et al (Immunochemical measurement of Early Pregnancy Isofoms of hCG: Potential Applications to Fertility Research, Prenatal Diagnosis, and Cancer, 32 (2001) 635-643) in view of Hochstrasser et al (US

2003/0157580) and Birken et al (US 6,521,416) as applied to claims 23-25, 42 and 43 above, and further in view of Campbell et al (US 4,946,958).

See above for teachings of O'Connor et al., Hochstrasser et al and Birken et al.

O'Connor et al., Hochstrasser et al and Birken et al differ from the instant invention in failing to teach the assay is a chmiluminescent sandwich assay.

Campbell et al disclose a chemiluminescent label which is conveniently linked to a monoclonal antibody or other protein and is used in immunoassay for the quantitation of an antigen of interest (abstract). Campbell et al disclose that the use of this chemiluminescent label in assays provides a means of improving the sensitivity of measurement of proteins and polypeptides by one to two orders of magnitude (col 7, lines 27).

It would have been obvious to one of ordinary skill in the art to substitute the chemiluminescent label as taught by Campbell et al for the label of O'Connor et al because Campbell et al shows that the use of this chemiluminescent label in two-site assays provides a means of improving the sensitivity of measurement of proteins and polypeptides by one to two orders of magnitude.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
March 1, 2005

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03/04/05